SOP 330 Monitoring Clinical Trials of an Investigational Medicinal Product and Device Trials

For Use in:	Research & Development
By:	All staff
For:	All staff involved in the conduct of research
Division responsible for document:	Research & Development
Key words:	Monitoring
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Date of approval:	07 August 2019
To be reviewed before: This document remains current after this date but will be under review	07 August 2022 (3 years from issue unless legislation or process changes)
Reference and / or Trust Docs ID No:	13485
Version No:	1.5
Description of changes:	Template change Guidance updates

This Standard Operating Procedure (SOP) is available on the Research & Development pages on the NNUH website

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1. Contents

2. Definitions of Terms Used / Glossary

Central or Remote monitoring	**Monitoring activities undertaken by the monitoring personnel in a location remote from the investigator site (for example, a data centre).**
CI	**Chief Investigator**
CRF	**Case Report Form**
CTIMP	**Clinical Trial of an Investigational Medicinal Product**
GCP	**Good Clinical Practice**
Likelihood	**The state or fact of something being likely. Probability**
Monitoring Plan	**A description of the methods, responsibilities and requirements for monitoring the trial, according to the Integrated Addendum in GCP E6 (R2)**
Monitoring Report	**A written report from the monitor to the sponsor after each site visit.**
NCTU	**Norwich Clinical Trials Unit**
NNUH	**Norfolk and Norwich University Hospital**
On site Monitoring	**Monitoring activities primarily undertaken during a physical visit to the investigator site by one or more monitoring personnel**
PI	**Principal Investigator**
QC	**Quality Control**
R&D	**Research and Development**
SDV	**Source Data Verification: An important part of monitoring is to compare the entries in case report forms (CRFs) with the original source documents (e.g. patient notes, test results).**
SIV	**Site Initiation Visit**

SOP	**Standard Operating Procedure**
TMF	**Trial Master File**
UEA	**University of East Anglia**

3. Scope

This SOP describes the process and responsibilities for the monitoring of Clinical Trials of an Investigational Medicinal Product (CTIMPs) and Device Trials Sponsored by the Norfolk and Norwich University Hospitals NHS Foundation Trust.

4. Introduction

Monitoring is an integral process in the Quality Control (QC) of a trial. Monitoring ensures that a trial it is conducted, recorded, and reported in accordance with the trial protocol, applicable SOPs, policies, GCP, and the applicable regulatory requirement(s) (section 1.38 ICH Guideline for Good Clinical Practice E6 (R2), dated 9 November 2016.)

According to the principles of ICH GCP (section 5.18.1, ICH Guideline for Good Clinical Practice E6 (R2), dated 9 November 2016.) the purposes of trial monitoring is to verify that:

- The rights and well–being of human subjects are protected.
- The reported trial data are accurate, complete and verifiable from source documents.
- The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).

Monitoring is part of a multi-factor approach to ensure the quality of research for all NNUH sponsored CTIMPs and Device Trials. Monitoring may take place by on-site visits or by centralized / remote monitoring, or a combination of the two.

For the monitoring of NNUH Sponsored studies that are not classified as CTIMPs or Device Trials.

- Refer to the **Guidance Document for Sponsor oversight of non-CTIMPS, non- Device Trials Sponsored by Norfolk and Norwich University Hospitals NHS Foundation Trust**
- Guidance document located in EDGE - https://www.edge.nhs.uk/Home/GeneralDocuments - Sponsor Oversight Visit.

5. Responsibilities

Sponsor

- Overall management of trial
- Selection of monitoring personnel
- Ensure that the monitor is appropriately qualified and trained to monitor the trial adequately
- Determine the extent and nature of monitoring required based on review of the risk assessment for the study.
- Approve the trial specific risk adapted monitoring plan

Monitor

- Act as the main line of communication between the sponsor and the investigator
- Ensure a trial specific monitoring plan is developed proportionate to the requirements of the study and its level of risk
- Comply with the monitoring plan, and ensure that any deviations have prior approval of the Sponsor.

For further information for NNUH Monitors refer to the Working Process Document WPD010 Monitors Guide to the Monitoring of Clinical Trials of an Investigational Medicinal Product and Device Trials.

Chief Investigator / Principal Investigator

- Review and agree the monitoring plan
- Facilitate monitoring access for the study
- Ensure that all essential documents/source data/ participant information is available for inspection at monitoring visits
- Receive monitoring reports
- Act on any issues identified in the monitoring reports, as appropriate
- Respond to monitor requests for completion/correction of data
- Co-ordinate trial management to facilitate central, remote and/or site monitoring

Third Parties Involved

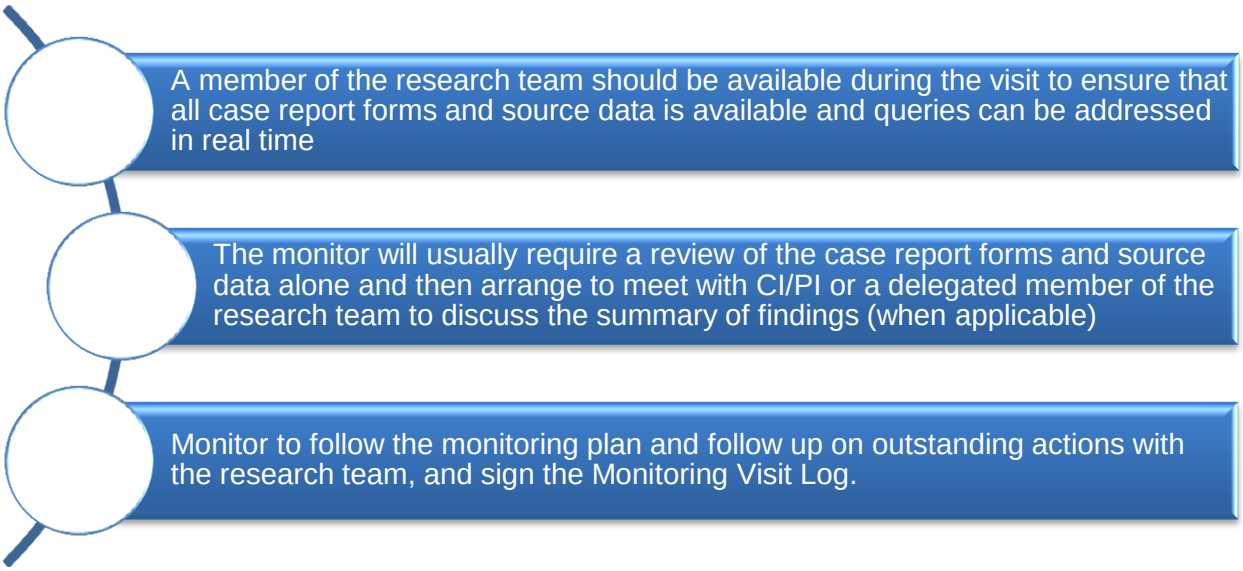
- Facilitate monitoring visits and allow access to study related documentation
- Act on any issues identified in the monitoring reports, as appropriate
- Respond to monitoring requests

6. Process for NNUH Monitored Studies

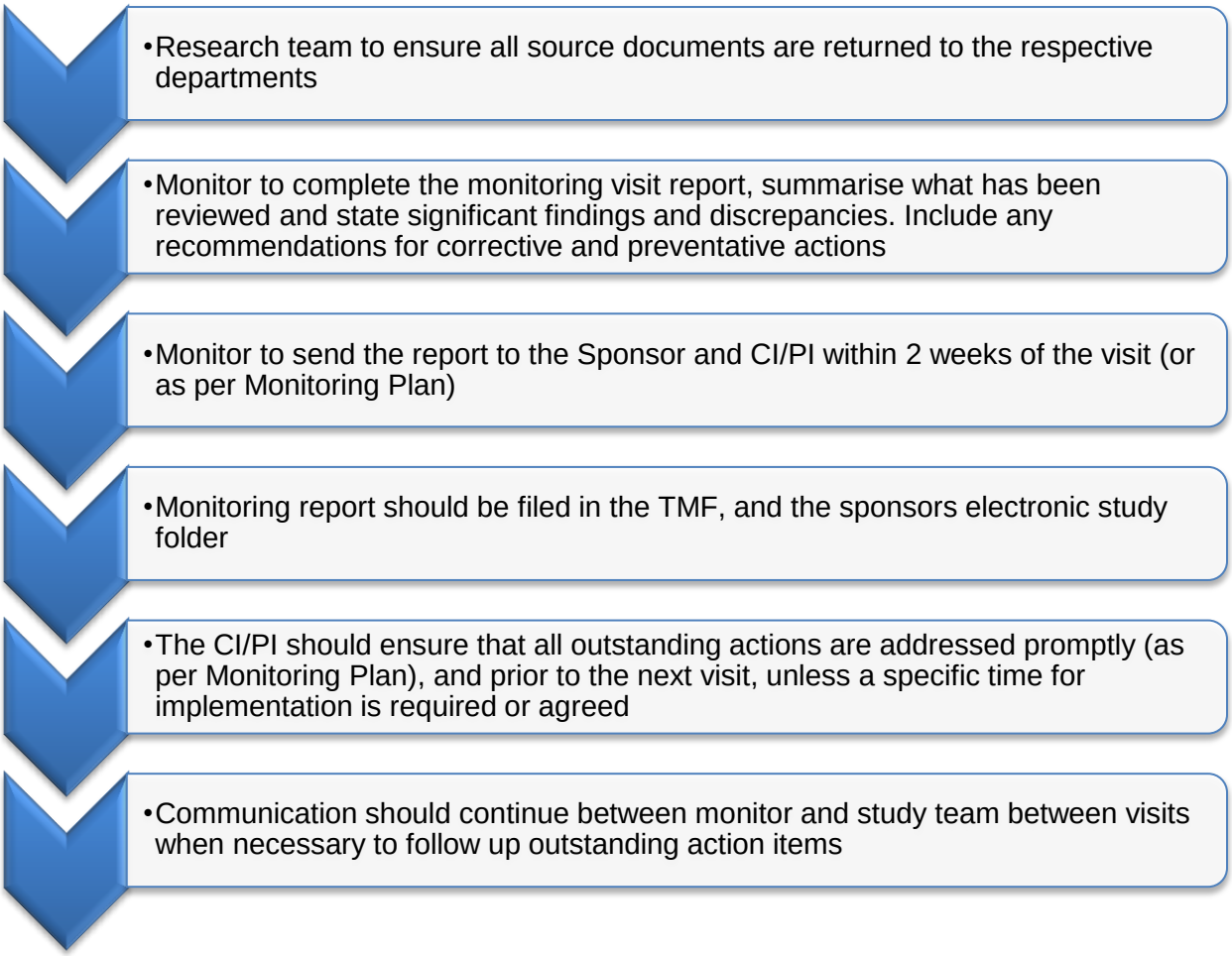
6a. Preparing for a Monitoring Visit

- The monitor will inform the research team where, when and for how long the visit will take place
- The site file, all case report forms and source documents should be available for monitoring visits
- If large numbers of patients have been recruited the monitor should agree with the research team which patient files will be required for reviewed prior to the visit
- The monitor will inform the CI and PI of the schedule of monitoring visits
- The monitor will arrange with the research team for a room/desk to be available for the visit
- If other departments (e.g. pharmacy) are to be visited they should be informed and arrangements made to review the files and or equipment & facilities
- A study initiation visit (SIV) should take place before recruitment begins at the site
- Refer to SOP 410 Set up and Initiation of an Investigator Site

6b. During a Monitoring Visit



6c. Following the Monitoring Visit



Adhoc Monitoring Visits

- If during the course of a study circumstances arise which warrant additional monitoring, an adhoc monitoring visit will be arranged, and whenever possible, carried out following the same process as a planned visit. The Sponsor should approve the adhoc visit and reasons for the visit documented in the adhoc monitoring visit report.

7. Closure of the study

Following notification to the Sponsor of last patient last visit, all the data have been collected (there are no more outstanding AEs/SAEs & all outstanding Queries/data clarification forms have been resolved appropriately), the database is locked and ready for statistical analysis, and the study conduct has ended, the monitor should arrange a final close-down visit. This is to ensure that all essential documents at site are complete and reconciled, any outstanding follow-up or corrective actions are completed by the study team, that drug accountability and or equipment accountability (when applicable) is complete and to ensure that data is prepared for archiving.

Site close-down visits are mandatory and it is the responsibility of the CI to ensure that these occur for sites that have been activated (i.e. site initiation took place). A close-down report will be completed by monitor after the visit and a copy of this will be filed in the TMF and investigator site file.

In the event of site close down resulting from early study termination, refer to **SOP 335 Research Project Closure (Including procedure or Project suspension or early termination)** for more information.

Norwich Clinical Trials Unit Monitored Studies

- For either NNUH sponsored studies or UEA sponsored studies, where the Norwich Clinical Trials Unit (NCTU) has been delegated the responsibility of study monitoring, NCTU monitoring processes and documentation will apply.

8. Approval

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9. Reason for Update and Training Implication

This replaces SOP 330 V1.4

Update	Reason	Training Implication	Action
Update to SOP Template, update to SOP name, inclusion of Device Trials, addition of template documentation in EDGE, and the removal of monitoring of non CTIMPs non device trials, which is now in a guidance document referenced within this SOP.	SOP required updating	Yes	Review SOP and update training matrix.